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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/786,055	03/01/2001	Christian Belmant	BE 8992	6944

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EXAMINER	
SCHNIZER, RICHARD A	

ART UNIT	PAPER NUMBER
1635	9

DATE MAILED: 08/27/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/786,055	BELMANT ET AL.	
	Examiner	Art Unit	
	Richard Schnizer, Ph. D	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *19 June 2003* .

2a)☒ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *29-84* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *29-84* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on _____ is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

An amendment was received and entered as Paper No. 8 on 6/19/03.

Originally filed claims 1-28 were canceled and new claims 29-84 were added as requested.

Claims 29-84 are under consideration in this Office Action.

This Action is NON-FINAL due to new grounds of rejection not necessitated by amendment, e.g. the written description rejection, and indefiniteness rejections over the nature of the claimed compounds.

Specification

The application is objected to because of alterations which have not been initialed and/or dated as is required by 37 CFR 1.52(c). See page 24, line14, and page 34, line 23. A properly executed oath or declaration which complies with 37 CFR 1.67(a) and identifies the application by application number and filing date is required.

Claim Objections

Claim 38 is objected to because "corporal" is misspelled.

Claim 58 is objected to because the 'h' in "ph" should be capitalized to represent hydrogen ion concentration.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 29, 31-41, 44-47, 49, 51-62, and 64-84 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 29, 31-42, 45, 47, 49, 52, 54-62, 64, 67, 69-75, 77, 80, and 82-84 are indefinite because the claims do not particularly and distinctly claim the subject matter which is the invention. More specifically, these claims are drawn to genuses of compounds having a phosphoepoxide group, but it is not clear to what the phosphoepoxide group may be attached. The structural description of the phosphoepoxide group shows a bond on the terminal phosphate oxygen to which, presumably, something is bound. However, it is not clear from the claims what , if anything, is on the other end of this bond. If nothing is on the other end then, then there can be no bond, only an unbonded pair of electrons. If there is an entity on the other end of the bond, the claims do not particularly and distinctly point out what it is.

Claims 29 and 31-41 are indefinite because it is unclear what is intended by the phrase " an effective amount of a compound, at least one phosphoepoxide group". Deletion of the comma and substitution of the word --comprising-- therefor, is suggested.

Claims 44, 46, 51, 53, 66, 68, and 79 are indefinite because they recite chemical structures comprising 'X' and 'Y', but fail to define 'X' or 'Y'.

Claims 44, 46, 51, 53, 66, 68, and 79 are indefinite because the metes and bounds of "a substituent which does not prevent formation of the halohydrin function X-CH2-C(OH)(R1)-" are unclear. Similarly, the metes and bounds of "a substituent for which there is an R2-O-Y compound that is not reactive towards the halohydrin function" of the compound of formula (12) are unclear. Applicant has described the claimed subject matter by what it is not, rather than by what it is. While there is nothing inherently ambiguous or uncertain about a negative limitation, the boundaries of the patent protection sought must be set forth definitely. In this case, the claimed genus has only a functional limitation, and no structural limitations whatsoever. Because the specification makes no correlation between the structure and function of the claimed substituents, one of skill in the art cannot know the metes and bounds of the claimed genus.

Claim 56 is indefinite because it is unclear what are the metes and bounds of "a general route". The specification does not give this term a limiting definition, and a search of the prior art did not reveal it as a term of art, thus one of skill in the art could not know the metes and bounds of the claim.

Claim 65 is indefinite because it does not end in a period.

Claim 74 is indefinite because it is unclear what is intended by "injection diseases".

Claims 75-81 are indefinite because the metes and bounds of "cells sensitive to Tγ9δ2 lymphocytes" are unclear. The specification does not define "sensitive" in this context, so one of skill in the art cannot know the breadth of protection Applicant seeks.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

New Matter

Claims 30, 43, 44, 48, 50, 51, 58, 63, 65, 66, and 75-81are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claims 30, 43, 44, 48, 50, 51, 63, 65, 66, 76, 78, and 79 recite a phosphoepoxide structure in which the terminal phosphate contains to following structure: P-O-O^--Ca^+. The specification as filed provides no written support for this structure, and so it represents new matter. The Examiner believes that this is likely to be a typographical error, and the rejection can be overcome by deleting "O-" from the structure.

Claim 58 requires sterile buffer at pH 7. The specification discloses at page 22, lines 20 and 21 sterile phosphate buffer at pH 7, but fails to support the broader genus of *any* sterile buffer at pH 7.

Claim 74 recites "injection diseases". This term was not present in the specification or claims as filed and represents new matter.

New claims 75-81 recite "Tγ9δ9 lymphocytes". This term was not present in the specification or claims as filed and represents new matter.

Written Description

Claims 44, 46, 51, 53, 66, 68, and 79 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

These claims are drawn to the genus of substituents that do not prevent formation of the halohydrin function X-CH2-C(OH)(R1)-, or the genus of substituents R2-O-Y that are not reactive toward the halohydrin function of the compound of formula (12). In other words, the claims describe by functional limitation, but not by structural limitation, the claimed genuses of structures.

When examining genus claims for adequate written description, one must determine whether or not a representative number of species of the claimed genus has been described. Applicant is referred to the Guidelines on Written Description published at FR 66(4) 1099-1111 (January 5, 2001) (also available at www.uspto.gov). The following passage is particularly relevant.

> The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant identifying characteristics, i.e. structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between structure and function, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus.

> A "representative number of species" means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within a genus, one must describe a sufficient number of species to reflect the variation within the genus. What constitutes a "representative number" is an inverse function of the skill and knowledge in the art. Satisfactory disclosure of a "representative number" depends on whether one of skill in the art would recognize that applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed. In an unpredictable art, adequate written description of a genus which embraces widely variant species cannot be achieved by disclosing only one species within the genus.

The instant specification sets forth several classes of compounds within the claimed genus, e.g. nucleoside derivatives, oligonucleotides, nucleic acids, amino acids, peptides, proteins, mono-, oligo-, and polysaccharides, fatty acids, folic acid, tetrahydrofolate, phosphoric acids, inositol, vitamins, co-enzymes, flavonoids, aldehydes, halohydrins, phosphoepoxides, and epoxides. Of these, a nucleoside, and a phosphoepoxide are reduced to practice. See e.g. Examples 3 and 4 at pages 30-32. Although several classes other than phosphoepoxides and nucleosides are listed in the specification, there is no disclosure of correlation between the structure and function of the claimed genuses, i.e. the specification fails to describe what structural characteristics are required to meet the claimed functional requirements. As a result, the breadth of the claimed genus is unclear, and it cannot be said that a representative number of species has been described.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 47, 48, 54-57 and 59 are rejected under 35 U.S.C. 102(b) as being anticipated by Muehlbacher et al (Biochemistry 27:7315-7328, 1988).

Muehlbacher teaches a diphosphoepoxide according to formula (2) of claim 2. This is admitted in the specification at page 5, lines 17-24. Muehlbacher also teaches methods of making the compound. See "Synthesis of Inhibitors" at pages 7316-7321, particularly first and second full paragraphs in column 2 of page 7320.

Response to Arguments

Applicants arguments filed 6/19/03 have been fully considered but are not persuasive. The basis of Applicant's argument is that the compounds of Muehlbacher contain ammonium salts and are toxic, and therefore cannot be administered to a primate. This argument is unpersuasive because it lacks adequate support. First, Applicant has failed to show that the amount of ammonium alleged to be present in the composition of Muehlbacher would be toxic to any primate, and second, Applicant has failed to show that a toxic composition cannot be administered to a primate. In fact, toxic pharmacological compositions are constantly administered to primates, including for example, alcohol, cigarette smoke, and chemotherapeutic drugs. Because the basis of Applicant's argument lacks adequate support, the rejection is maintained.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 47 and 58 are rejected under 35 U.S.C. 103(a) as being unpatentable over Muehlbacher et al (Biochemistry 27:7315-7328, 1988).

Muehlbacher teaches a diphosphoepoxide according to formula (2) of claim 2. This is admitted in the specification at page 5, lines 17-24. Muehlbacher also teaches methods of making the compound. See "Synthesis of Inhibitors" at pages 7316-7321, particularly first and second full paragraphs in column 2 of page 7320. Muehlbacher also teaches a composition comprising an aqueous buffer of pH 7 and the compound. Aqueous solutions comprising the compound were diluted with a stock solution of 5mM HEPES, pH7. See e.g. fourth full paragraph on page 2722.

Muehlbacher is silent as to whether the buffer is sterile.

It would have been obvious to one of ordinary skill in the art at the time of the invention to use a sterile stock of buffered solution in the invention of Muehlbacher. One would have been motivated to do so in order to ensure that microorganisms such as mold or fungi did not grow in the stock solution. Thus the invention as a whole was prima facie obvious.

Conclusion

No claim is allowed. Claims 29-46, 49-53 and 60-84 are free of the prior art of record.

Any inquiry concerning this communication or earlier communications from the examiner(s) should be directed to Richard Schnizer, whose telephone number is 703-306-5441. The examiner can normally be reached Monday through Friday between the

hours of 6:20 AM and 3:50 PM. The examiner is off on alternate Fridays, but is sometimes in the office anyway.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John Leguyader, can be reached at 703-308-0447. The FAX numbers for art unit 1632 are 703-308-4242, and 703-305-3014. Additionally correspondence can be transmitted to the following RIGHTFAX numbers: 703-872-9306 for correspondence before final rejection, and 703-872-9307 for correspondence after final rejection.

Inquiries of a general nature or relating to the status of the application should be directed to the Patent Analyst Trina Turner whose telephone number is 703-305-3413.

Richard Schnizer, Ph.D.

DAVE T. NGUYEN
PRIMARY EXAMINER